REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks. Applicants respectfully thank the Examiner for holding a telephone interview with Applicants' representative. The Examiner's kind suggestions have been incorporated herein.

I. CLAIM STATUS AND AMENDMENTS

Claims 1 and 4-18 were pending in this application when last examined.

Claim 18 was withdrawn as non-elected subject matter. Applicants reserve the right to file a Continuation or Divisional Application on any non-elected subject matter.

Claims 13 and 15-17 are amended to clarify the claimed invention.

Claim 14 is cancelled without prejudice or disclaimer thereto.

No new matter has been added.

II. DOUBLE PATENTING REJECTIONS

On page 3 of the Office Action, claims 1, 4, 6-7 and 17 were provisionally rejected on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 and 18-21 of U.S. Application 10/926,088.

As noted during the telephonic interview, the claims of the present application are directed towards full-length HGF. On the other hand, the cited application discloses a segment of HGF α-chain.

Thus, the present invention and application Serial No.10/926,088 disclose different molecules. The present invention discloses glycosylation deficient HGF, which is an agonist of c-Met receptor tyrosine kinase. On the other hand, application Serial No.10/926,088 discloses a segment of glyosylation deficient HGF α-chain, of which molecular weight is much smaller than HGF. A segment of glyosylation deficient HGF α-chain is an antagonist of c-Met receptor tyrosine kinase, which has an opposite activity to HGF.

Thus, this rejection is untenable and should be withdrawn.

III. 35 U.S.C. § 112 REJECTIONS

On page 4, claim 17 was rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification lacks written description support for non-glycosylated HGF as an active ingredient in combination with a conventional carrier or a binder.

This rejection is overcome, as applied to amended claim 17, for reasons which are self-evident. Applicants note that such was confirmed during the above-noted telephone interview.

Further, on pages 4-5 of the Office Action, claims 13-16 were rejected 35 U.S.C. § 112, second paragraph, as indefinite. Applicants note that this rejection, as applied to the remaining amended claims, is overcome as the claims have been amended to remove reference to "having no sugar chains". Further, claim 14 is cancelled without prejudice or disclaimer thereto.

Thus, as noted during the telephone interview, this rejection is overcome.

IV. OBVIOUSNESS REJECTIONS

On pages 5-7, claims 1, 4, 6-15 and 17 were rejected under 35 U.S.C. § 103(a) as obvious over Godowski et al. (US 5,316,921) in view of Shimizu (BBRC, 1992). Further, on page 7, claims 1, 4-15 and 17 were rejected under 35 U.S.C. § 103(a) as obvious over Godowski et al. in view of Shimizu and further in view of Miyake et al. (US 7,125,688) and Miyake et al. (US 7,129,064). Finally, on page 8, claims 1,4, and 6-17 were rejected under 35 U.S.C. § 103(a) as obvious over Godowski et al. in view of Shimizu and further in view of Patten et al. (US 6,365,377).

Applicants respectfully traverse these rejections.

(i) Invention of present claim 1

Present claim 1 recites a glycosylation-deficient hepatocyte growth factor having no sugar chains and having mutations in its amino acid sequence so that no glycosylation occurs at any glycosylation sites of the hepatocyte growth factor.

(ii) Cited reference Godowski

The Examiner states that it would have been obvious to produce HGF that was completely carbohydrate free by mutating each glycosylation site so that it was not capable of glycosylation as suggested by Godowski et al.

However, Examiner's statement is not correct.

Godowski neither discloses nor suggests a completely carbohydrate free HGF. Further, in addition, Godowski neither discloses nor suggests amino acid mutation so that no glycosylation occurs.

Specifically, HGF has four N-linked glycosylation sites and one O-linked glycosylation site, as evidenced by the specification of the present application, page 18, lines 2-14.

Regarding N-linked glycosylation of HGF, Godowski merely mentions recognition sequences for enzymatic attachment of the carbohydrate moiety to the asparagine side chains (column 14, lines 19-22). Godowski neither discloses nor suggests mutation of the recognition sequences so that no N-linked glycosylation occurs.

Regarding O-linked glycosylation of HGF, Godowski mentions that O-linked glycosylation sites may be modified by the addition of, or substitution by, one or more serine or threonine residue to the amino acid sequence of the HGF molecule (column 14, lines 37-40). According to Godowski, extra serine or threonine may be inserted to the amino acid sequence. The insertion of serine or threonine means that extra O-linked glycosylation occurs. Please see Godowski, column 14, lines 35-37. Thus, the present invention and Godowski make a sharp contrast in the occurrence of O-linked glycosylation: the present invention relates to no glycosylation, while Godowski teaches increases in glycosylation sites.

Therefore, Godowski neither discloses nor suggests amino acid mutation so that no glycosylation occurs.

(iii) Cited reference Shimizu

Furthermore, Shimizu neither discloses nor suggests amino acid mutation so that no glycosylation occurs. Shimizu merely mentions O-glycanase treated HGF, which lacks O-glycosylation (page 1334, lines 27-29) , contrary to the claimed invention.

In addition, Shimizu neither discloses nor suggests a completely carbohydrate free HGF, since Shimizu merely mentions O-glycosylation-lacking HGF. Shimizu is silent regarding the lack of N-linked glycosylation, which is essential for the claimed invention of the application.

Therefore, the inventions of claim 1 and claims 4, 6-15 and 17 depending on claim 1 are unobvious from Godowski and Shimizu.

Further, as the Examiner mentions, Miyake (USP No. 7,125,688) and Miyake (USP No. 7,129,064) merely disclose methods of producing feline and canine HGF in E. coli, respectively, and Patten merely discloses recombinantly producing HGF in a cell free system such as an

E. coli lysate.

Any of Miyake (USP No. 7,125,688), Miyake (USP No. 7,129,064) and Patten does not fill the gap between the invention of present claim 1 and the disclosure of Godowski and Shimizu, which is described above. In other words, none of the cited references teach or suggest the mutated non-glycosylated HGF of the claimed invention.

Therefore, the inventions of Claims 1 and 4-17 are unobvious from these cited references.

Thus, for the above noted reasons, these rejections are untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Toshikazu NAKAMURA et al.

/William R. Schmidt, II/

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